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| EXAMINER | |
|---|---|
| SHIBUYA, MARK LANCE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1639 | |

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|---|---|
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/506,756 | KOZLOWSKI ET AL. | |
| | Examiner | Art Unit | |
| | Mark L. Shibuya, Ph.D. | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *8-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Application 10506756, (20050181449 A1): Claims 1-15 are pending. Claims 8-15 are withdrawn from consideration. Claims 1-7 are examined.

### *Election/Restrictions*

2. Applicant's election of Group I, claims 1-7 and the species of "cytosolic accessory proteins of ion-channels" in the reply filed on 9/20/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 7-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/20/2007.

### *Priority*

4. Application 10/506,756 is the national stage of PCT/GB03/01049, filed 3/13/2003, under 35 U.S.C. 371. This application claims foreign priority to United Kingdom priority document 0205910.3, filed 3/13/2002.

### *Specification*

5. The disclosure is objected to because of the following informalities: The specification at pp. 30-31 discloses polypeptide sequences that must be identified by sequence identifiers. Appropriate correction is necessary.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 states the term “it's” and “it” in lines 2 and 3, respectively, which render the claim vague and indefinite because (1) it is not clear what claim element “it's” refers 2to and (2) “it's” is a contraction of “it is”.

The term "normally" in claim 1 is a relative term which renders the claim indefinite. The term "normally" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree of “normally complexed”, and one of skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Claims 1 recites the limitation "it's membrane protein components" in line 2. There is insufficient antecedent basis for this limitation in the claim because it is unclear that a cytosolic accessory protein possesses inherently components that are *membrane* protein components.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Kornbluth et al., US 20020188104 A1, (of record), and as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, (of record); Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, (of record); or Zarsky et al., FEBS Letters (1997) vol. 403, 303-308), (of record).

The claims are drawn to an array comprising a surface having attached thereto at least one cytosolic accessory protein free of it's membrane protein components or other subunits with which it is normally complexed.

Kornbluth et al., US 20020188104 A1, (of record), discloses arrays (96 well plates) containing isolated cytosol, which would inherently comprise cytosolic accessory proteins, (as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, at, e.g., p. 43; Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, at e.g., the abstract; Zarsky et al., FEBS Letters (1997) vol. 403, 303-308, at, e.g., the abstract).

Kornbluth et al. states:

> [0070] In addition to the above-described binding assays, function-based assays can also be used to screen test compounds for potential use as hRpr agonists or antagonists. Compounds that enhance or inhibit hRpr-induced apoptosis can be screened for based on the observation that hRpr, like its Drosophila counterpart, can act in conjunction with cytosolic factors to trigger cytochrome c release from the mitochondria (Evans et al, EMBO J. 16:7372-7381 (1997)). For example, mitochondria purified from Xenopus egg extracts can be aliquoted into 96-well plates. Isolated cytosol (e.g., prepared in parallel from Xenopus eggs) or cytosol immunodepleted of the hRpr-interacting protein, Scythe, can be added to the wells. This array can then be used to screen test compounds for their ability to trigger cytochrome c release from mitochondria in the presence of Scythe (i.e., Reaper-mimetics) or to screen test compounds for their ability to enhance or inhibit cytochrome c release upon addition of hRpr (e.g., recombinant). Cytochrome c release can be measured via an ELISA using anti-cytochrome c antibodies or fluorometrically using mitochondria pre-loaded with GFP-cytochrome c (Goldstein et al, Nature Cell Biol. 2:156 (2000)).

Kornbluth et al. at p. 5, para [0070]. Thus Kornbluth teaches arrays of cytosol depleted of hRpr-interacting protein for use in an array to test compounds, which release cytochrome c from mitochondria, which are membrane-bound organelles.

Furthermore, absent evidence to the contrary, the examiner respectfully submits that the cytosolic array of Kornbluth would, comprise accessory proteins to membrane proteins, as evidenced by Shisheva, Leung et al., and Zarsky et al.

Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, at, e.g., p. 43 discloses accessory proteins that are GDP dissociation inhibitor (GDI) proteins required for Rab function and progression through membrane/cytosol localization cycle and recycling. Shisheva, at p. 40, disclose that Rabs are hydrophobic peripheral membrane proteins and that GDI genes encode highly homologous protein isoforms, reading on families. Rab proteins are G family proteins.

Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), pp. 2607-2614, at e.g., the abstract teach a purified 16-kDa cytosolic protein (p16) accessory protein to heat shock cognate protein Hsc70. p16 is a member of the Nm23/nucleoside diphosphate (NDP) kinase family. Leung et al., at p. 2607, states that Hsc70 is involved in targeting proteins to lysosomes for degradation and in importing cytoplasmic proteins into the nucleus. Leung et al., at p. 2613, teach that NDP kinase associate with proteins that require guanine nucleotides for function, including GTP (G) proteins. The examiner respectfully submits that NDP kinases also describe accessory proteins to G proteins.

Zarsky et al., FEBS Letters (1997) vol. 403, 303-308, at, e.g., the abstract, teach Rab accessory proteins.

11. Claims 1-7 are rejected under 35 U.S.C. 102(e) as being anticipated by Charych et al, US 20020055125 A1, (of record), and as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, (of record); Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, (of record); or Zarsky et al., FEBS Letters (1997) vol. 403, 303-308), (of record).

Charych et al., US 20020055125 A1, throughout the publication, discloses arrays of samples derived from cytosol, which would inherently comprise cytosolic accessory proteins, (as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50; Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614; or Zarsky et al., FEBS Letters (1997) vol. 403, 303-308).

Charych et al., state:

> [0104] In particular, arrays in accordance with the present invention are useful in performing proteomic analyses of complex protein samples. As used herein, proteomics is the separation and/or quantitation and/or identification of one or more proteins in a sample. The sample may be derived from a cell (e.g., the cell's cytosol, membrane or extra-cellular proteins), tissues (e.g., dissected or laser-microdissected), body fluids (such as urine, blood spinal fluid) or any other sample containing proteins. The results of such separation/quantitation/identification may produce novel protein targets for drug screening, proteins for diagnostics, or novel synthetic ligands for assays or protein purification. The arrays may very effectively be used in differential protein binding assays. For example, two (or more)-color fluorescent labeling of complex protein mixtures, and the analysis of differential protein binding to the array by fluorescence imaging may be conducted. As described below, the arrays may be used in conjunction with other techniques to identify, sequence and structurally characterize differentially expressed proteins or peptides of interest. The arrays may be run in parallel with DNA arrays and the differential binding results compared to identify correlations between gene activity and protein expression. Also, mixed arrays, wherein the molecules making up an array includes antibodies, etc. may be prepared and used to conduct binding assays.

Charych et al., at para [0104]. Thus Charych teaches arrays of cytosol proteins for use in differential protein binding assays. Charych teaches identifying, sequencing and structurally characterizing proteins or peptides of interest.

Furthermore, absent evidence to the contrary, the examiner respectfully submits that the cytosolic array of Charych would, comprise accessory proteins to membrane proteins, as evidenced by Shisheva, Leung et al., and Zarsky et al.

Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, at, e.g., p. 43 discloses accessory proteins that are GDP dissociation inhibitor (GDI) proteins required for Rab function and progression through membrane/cytosol localization cycle and recycling. Shisheva, at p. 40, disclose that Rabs are hydrophobic peripheral membrane proteins and that GDI genes encode highly homologous protein isoforms, reading on families. Rab proteins are G family proteins.

Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), pp. 2607-2614, at e.g., the abstract teach a purified 16-kDa cytosolic protein (p16) accessory protein to heat shock cognate protein Hsc70. p16 is a member of the Nm23/nucleoside diphosphate (NDP) kinase family. Leung et al., at p. 2607, states that Hsc70 is involved in targeting proteins to lysosomes for degradation and in importing cytoplasmic proteins into the nucleus. Leung et al., at p. 2613, teach that NDP kinase associate with proteins that require guanine nucleotides for function, including GTP (G) proteins. The examiner respectfully submits that NDP kinases also describe accessory proteins to G proteins.

Zarsky et al., FEBS Letters (1997) vol. 403, 303-308, at, e.g., the abstract, teach Rab accessory proteins.

12. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Patron et al., US 20010041349 A1, (of record), and as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, (of record); Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, (of record); or Zarsky et al., FEBS Letters (1997) vol. 403, 303-308), (of record).

Patron et al., US 20010041349 A1, throughout the publication, disclose arrays of recombinant cytosolic proteins, which would inherently comprise cytosolic accessory proteins, (as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, at, e.g., p. 43; Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, at e.g., the abstract; Zarsky et al., FEBS Letters (1997) vol. 403, 303-308, at, e.g., the abstract).

Patron et al., states:

> [0041] Recombinant proteins may be assayed either in the expression array, or after transfer of the proteins to a second array format. For example, an array of protein expression systems may be distributed in the wells of a microtiter-like array. Referring now to FIG. 3, in the case of soluble protein 40 secreted from cells 42, the presence of the protein may be evaluated directly in the well 46, or after transfer of the secreted components to another well 48 (FIG. 3A, bottom and top panels, respectively). Similarly, where the soluble protein is cytosolic, the cells may be lysed and the recombinant protein measured directly in the well, or after transfer of the secreted components to another well. In either case, detection of expressed protein does not compromise isolation of the plasmid/phagemid DNA from each site of the array. Thus, for the array site which provides an interaction of interest, the recombinant DNA can be isolated and propagated for further characterization.

Patron et al., at para [0041]. Patron at para [0020] teach immobilized proteins wherein the proteins are of the same family and wherein the family includes intracellular signal

transduction modulators and effectors, apoptosis-related factors and other factors, reading on accessory proteins.

13. Claims 1-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al., WO 0004382 A1, and as evidenced by Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, (of record); Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), 2607-2614, (of record); or Zarsky et al., FEBS Letters (1997) vol. 403, 303-308), (of record).

Wagner et al., WO 0004382 A1, throughout the publication, and abstract, and at pp. 15-18, teach arrays of proteins, and wherein the arrayed proteins are of a protein family. Wagner et al., at pp. 17-18, bridging paragraph, disclose examples of protein families. Wagner et al. state:

> The proteins immobilized on the array of the invention may be members of a protein family such as a receptor family (examples: growth factor receptors, catecholamine receptors, amino acid derivative receptors, cytokine receptors, lectins), ligand family (examples: cytokines, serpins), enzyme family (examples: proteases, kinases, phosphatases, ras-like GTPases, hydrolases), and transcription factors (examples: steroid hormone receptors, heat-shock transcription factors, zinc-finger, leucine-zipper, homeodomain). In one embodiment, the different immobilized proteins are all HIV proteases or hepatitis C virus (HCV) proteases. In an alternative embodiment, the protein immobilized on each patch is a different antibody or antibody fragment (Fab, for example).

Wagner et al., at pp. 17-18, bridging paragraph.

Wagner et al., at p. 48, teach interactions that include receptor/effector protein relationships, reading on accessory protein binding interaction. Wagner, at Examples 9

and 10, teaches immobilizing soluble proteins to an array by means of immobilized antibody fragments.

Furthermore, absent evidence to the contrary, the examiner respectfully submits that the cytosolic array of Wagner would, comprise accessory proteins to membrane proteins, as evidenced by Shisheva, Leung et al., and Zarsky et al.

Shisheva, Methods In Enzymology, (2001), Vol. 329, 39-50, at, e.g., p. 43 discloses accessory proteins that are GDP dissociation inhibitor (GDI) proteins required for Rab function and progression through membrane/cytosol localization cycle and recycling. Shisheva, at p. 40, disclose that Rabs are hydrophobic peripheral membrane proteins and that GDI genes encode highly homologous protein isoforms, reading on families. Rab proteins are G family proteins.

Leung et al., J. Biol. Chem. (Jan. 31, 1997), Vol. 272 (5), pp. 2607-2614, at e.g., the abstract teach a purified 16-kDa cytosolic protein (p16) accessory protein to heat shock cognate protein Hsc70. p16 is a member of the Nm23/nucleoside diphosphate (NDP) kinase family. Leung et al., at p. 2607, states that Hsc70 is involved in targeting proteins to lysosomes for degradation and in importing cytoplasmic proteins into the nucleus. Leung et al., at p. 2613, teach that NDP kinase associate with proteins that require guanine nucleotides for function, including GTP (G) proteins. The examiner respectfully submits that NDP kinases also describe accessory proteins to G proteins.

Zarsky et al., FEBS Letters (1997) vol. 403, 303-308, at, e.g., the abstract, teach Rab accessory proteins.

***Conclusion***

14. Claims 1-7 are rejected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Doug Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Primary Examiner
Art Unit 1639